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Factors Contributing and Leading to Miscarriages

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Abstract:
The purpose of study was to observe and record the factors leading to miscarriage.It was an observational study of 35 women who had suffered pregnancy loss(miscarriage). A study was conducted in Sir Ganga Ram Hospital Lahore to observe the factors leading to miscarriage.For this purpose,data of 35 patients was collected. Common factors leading to miscarriage were analyzed and recorded.The factors were tabulated and represented in the form of graphs. Data analysis revealed mal-nutrition,infection,intra-uterine devices,depression,hypertension,ectopic pregnancy,sexually transmitted diseses are the major factors contributing to miscarriage.

Key Words: Sexually transmitted diseases, Menstrual history, Mal-nutrition, Gynecological problems, Hysterectomy.

INTRODUCTION: A miscarriage is the loss (death) of a baby before the 20th week of pregnancy. On epidemiological evidence, the definition of recurrent miscarriage should be three or more consecutive pregnancy losses. Data should be collected to 28 weeks' gestation but analysis up to 20-22 weeks' or 500 g fetal weight should also be possible. General practitioners and gynaecologists should do what they feel is suitable for couples whose history does not meet these criteria but a diagnosis of recurrent miscarriage should not be made. Women meeting the definition can be subdivided into primary and secondary groups, respectively consisting of those who have lost all previous pregnancies and those who have had one successful pregnancy followed by consecutive losses.**(1)**

Human reproduction is extraordinarily wasteful. The reasons for this have taxed all of the contributors to this book. As we move into the 21st century it is sobering to reflect on the fact that we have failed to harness the power of the evolving revolution in molecular medical biology to answer the fundamental question: why is the fate of a fertilized egg so hazardous and so unsuccessful? The following account summarizes our limited knowledge of the epidemiology of miscarriage and then moves on to consider some of the medical causes of miscarriage. The contribution of genetic abnormalities to the problem of pregnancy wastage is discussed elsewhere in this volume.**(2)**

Fetal wastage has many causes, but genetic factors are by far the most common. The earlier the pregnancy loss occurs, the greater the likelihood of genetic causation. Among first trimester abortions, 50% to 80% show chromosomal abnormalities, usually aneuploidy. This is greater than all other causes combined. Chromosomal numerical abnormalities can be recurrent and sporadic; failure to take this into account is a major pitfall in many reports addressing causation. Moreover, many causes of fetal wastage that are traditionally considered to be nongenetic are actually the result of perturbations of gene products-proteins. Among nongenetic causes of first trimester fetal wastage, the best established are thyroid abnormities; antifetal antibodies; and the inherited and acquired thrombophilias. The latter are more established in the second trimester.

Uterine anomalies can lead to second trimester losses. Infections seem uncommon, and alloimmune causes are not validated.**(3)**

Use of visual display terminals (VDTs) was examined in a case-control study of pregnancy outcome among 1,583 pregnant women who attended three Kaiser Permanente obstetrics and gynecology clinics in Northern California,

1981-1982. author found a significantly elevated risk of miscarriage for working women who reported using VDTs for more than 20 hr per week during the first trimester of pregnancy compared to other working women who reported not using VDTs (odds ratio 1.8, 95% CI: 1.2-2.8). This risk could not be explained by age, education, occupation, smoking, alcohol consumption, or other maternal characteristics. No significantly elevated risk for birth defects was found among working women although odds ratios were 1.4 for both moderate and high VDT exposure, compared with no exposure (95% CI: 0.7-2.7 and 0.7-2.9, respectively). One possible explanation for these findings is that women who had adverse pregnancy outcomes may have overreported their exposures to VDTs and/or women with normal births may have underreported theirs. The findings may also be due to unmeasured factors confounded with high VDT use such as poor ergonomie conditions or job-related stress. That VDTs themselves are hazardous to the pregnant operator remains a possibility. The results underscore the need for large cohort studies of working women that will provide objective measures of VDT exposures, ergonomic factors, and stress.**(4)**

Recurrent miscarriage is a heterogeneous condition. While the role of acquired thrombophilia has been accepted as an etiology of recurrent miscarriage, the contribution of specific inherited thrombophilic genes to this disorder has remained controversial. compared the prevalence of 10 thrombophilic gene mutations among women with a history of recurrent miscarriages and fertile control women. A total of 150 women with a history of two or more recurrent pregnancy losses and 20 fertile control women with no history of pregnancy losses had buccal swabs taken for DNA analyses of 10 gene mutations [factor V G1691A, factor V H1299R (R2), factor V Y1702C, factor II prothrombin G20210A, factor XIII V34L, β-fibrinogen −455G>A, PAI-1 4G/5G, HPA1 a/b (L33P), MTHFR C677T, MTHFR A1298C]. The prevalence of these mutations was compared between women experiencing recurrent miscarriage and controls. No differences in the frequency of specific gene mutations were detected when women with recurrent miscarriage were compared with control women. However, the prevalence of homozygous mutations and total gene mutations among patients with recurrent miscarriage was significantly higher than among controls. Homozygous mutations were found in 59% of women with a history of recurrent pregnancy loss contrasted to 10% of control women. More than three gene mutations among the 10 genes studied were observed in 68% of women with recurrent miscarriage and 21% of controls. Inherited thrombophilias are associated with recurrent miscarriage. This association is manifest by total number of mutations rather than specific genes involved.**(5)**

The study was designed to determine whether clinical and endocrine characteristics assessed on initial screening of normogonadotropic oligo/amenorrhoeic infertile patients could predict ovulation and then conception and successful live birth or miscarriage.. A cumulative conception rate of 67% was reached after six or more CC-induced cycles. Patients with failure of ovulation after a full course of CC had more severe oligomenorrhoea ($p < 0.001$) and greater BMI ($p < 0.05$) at initial screening. There was no relationship with levels of LH or androgens. In contrast, among women who ovulated in response to CC, conception was associated with less frequent periods, and higher basal levels of LH, free testosterone and androstenedione. Conceptions with subsequent miscarriage were associated with intermediate levels of LH and numbers of spontaneous periods between non-conception and live births. These observations are consistent with the hypothesis that failure of ovulation after CC is related to different factors (overweight and severe oligomenorrhoea) from those that predispose to non-conception (low basal LH and androgen levels and mild oligomenorrhoea).**(6)**

It was objectified to investigate the endocrinological and endometrial factors in women with unexplained recurrent

miscarriage.. One hundred and forty-four women with unexplained recurrent (≥ 3) miscarriages. A blood sample was obtained in early follicular phase (day 3–5) to measure follicle stimulating hormone, luteinising hormone, prolactin, androgens and thyroid function; daily blood/urine samples were obtained from mid-follicular phase to measure luteinising hormone until the luteinising hormone surge was identified; endometrial biopsy and a further blood sample for progesterone measurement were obtained in the mid-luteal phase. A transvaginal ultrasonography was performed to evaluate ovarian morphology. Hypersecretion of luteinising hormone or ultrasonographic features of polycystic ovarian disease was present in 8% and 7.8% of women, respectively. The free androgen index was elevated in 14.6% of subjects. In the mid-luteal phase, low progesterone level was found in 17.4% and delayed endometrial development was noted in 27.1% of women. Although women with recurrent miscarriage women and delayed endometrium had significantly lower progesterone levels than those with normal endometrial development, only 8/24 had mid-luteal progesterone levels below 30 nmol/L. Recurrent miscarriage was not associated with hyperprolactinaemia or abnormal thyroid function test. Endocrinological and endometrial abnormalities are present in about a quarter of women with unexplained recurrent miscarriage.**(7)**

Recently, several investigations concerning disadvantageous genetic factors in human reproduction have progressed. Inherited thrombophilia, such as factor V Leiden, prothrombin, and methylenetetrahydrofolate reductase mutations; gene polymorphisms of detoxification enzyme (CYP1A1); growth factors (insulin-like growth factor-I); and hormones such as angiotensinogen and CYP17 are involved in the pathogenesis of fetal growth restriction. The inherited thrombophilia, gene polymorphisms of coagulation and anticoagulation factor such as thrombomodulin, endothelial protein C receptor, plasminogen activator inhibitor 1, and factor XIII; human lymphocyte antigen (HLA-G); detoxification enzymes (glutathione-***S***-transferase M1); cytokines such as interleukin (IL) -1 and IL-6; hormones (CYP17); vasodilators (nitric oxide synthase 3); and vitamins (transcobalamin) are involved in the pathogenesis of sporadic and recurrent miscarriage. It is likely that a gene polymorphism or mutation susceptible to reproductive failure has a beneficial effect on the process of human reproduction with or without the environmental interaction. The factor V Leiden mutation has genetic advantages that are believed to be an improved implantation rate in in vitro fertilization and a reduction of maternal intrapartum blood loss. It has also been demonstrated that the CYP17 A2 allele has bidirectional effects on human reproduction, including increases in susceptibility to recurrent miscarriage and fetal growth enhancement.(8)

Obesity has become a major health problem worldwide and is also associated with adverse pregnancy outcome. The aim of this study was to assess the impact of obesity on the risk of miscarriage in the general public. This was a nested case–control study. The study population was identified from a maternity database. Obese [body mass index (BMI) >30 kg/m^2] women were compared with an age-matched control group with normal BMI (19–24.9 kg/m^2). Only primiparous women were included in the study to avoid including the subject more than once, and to be able to correctly identify recurrent miscarriages. The prevalence of a previous his**to**ry of early (6–12 weeks gestation), late (12–24 weeks gestation) and recurrent early miscarriages (REM) (more than three successive miscarriages <12 weeks) was compared between the two groups. A **to**tal of 1644 obese and 3288 age-matched normal weight controls with a mean age of 26.6 years [95% confidence interval (CI) 26.5–26.7] were included in the study. The risks of early miscarriage and REM were significantly higher among the obese patients (odds ratios 1.2 and 3.5, 95% CI 1.01–1.46 and 1.03–12.01, respectively; P = 0.04, for both]. Obesity is associated with increased risk of first trimester and recurrent miscarriage.(9)

Fetal chromosome abnormalities account for about 50% of first-trimester pregnancy losses. Most of these abnormalities are numerical abnormalities (86%) and a low percentage is caused by structural abnormalities (6%) or other genetic mechanisms, including chromosome mosaicism (8%). The recurrence risk of numerical abnormalities is low, so karyotyping of fetal material in case of a miscarriage does not seem worthwhile in daily practice.Half of the structural abnormalities may be inherited from a parent carrying a balanced chromosome translocation or inversion. Parental carriership is found in 4–6% of the couples with recurrent miscarriage. In case of parental carriership of a balanced structural chromosome abnormality, a next pregnancy may result in a child with an unbalanced structural chromosome abnormality. This child can have multiple congenital malformations and/or a mental handicap. Prenatal diagnosis is therefore recommended.Conventional laboratory techniques, such as tissue culturing and karyotyping, or (semi-)direct chromosome technique of chorionic villi, and the recently developed laboratory techniques such as fluorescence in situ hybridization (FISH) and comparative genomic hybridization (CGH), are described successively.Until now, not enough evidence has been available about the role of other genetic mechanisms, such as single-gene abnormalities, uniparental disomy, genomic imprinting, multifactorial disorders and skewed X chromosome, in the occurrence of miscarriages.(10)

The study was desighned to evaluate whether prenatal use of non-steroidal anti-inflammatory drugs (NSAIDs) is associated with increased risk of miscarriage. Population based cohort study. Prenatal use of NSAIDs, aspirin, and paracetamol (acetaminophen) ascertained by in-person interview. 1055 pregnant women recruited and interviewed immediately after their positive pregnancy test. Median gestational age at entry to the study was 40 days. Pregnancy outcomes up to 20 weeks of gestation. 53 women (5%) reported prenatal NSAID use around conception or during pregnancy. After adjustment for potential confounders, prenatal NSAID use was associated with an 80% increased risk of miscarriage (adjusted hazard ratio 1.8 (95% confidence interval 1.0 to 3.2)). The association was stronger if the initial NSAID use was around the time of conception or if NSAID use lasted more than a week. Prenatal aspirin use was similarly associated with an increased risk of miscarriage. However, prenatal use of paracetamol, pharmacologically different from NSAIDs and aspirin, was not associated with increased risk of miscarriage regardless of timing and duration of use. Prenatal use of NSAIDs and aspirin increased the risk of miscarriage. These findings need confirmation in studies designed specifically to examine the apparent association.(11)

Aim of study was to evaluate and recored the factors contributing and leading to miscarriage enlisting 35 patients.

MATERIALS AND METHODS*:*

The study was conducted at Sir Ganga Ram Hospital Lahore enlisting 35 pregnant women.The patients fulfilling these inclusion criteria: pregnant woment,women who are pregnant or who have lost their pregnancy,pregnant women who have gynecological problems.The following patients were excluded from study:non pregnant women,women who have undergone hysterectomy.

RESULTS AND DISCUSSION:

During the study,case histories of 35 patients were considered having lost their pregnancy.Case history of 35 patienrs was evaluated to determinf and record the factors leading to miscarriage. The age group found most susceptible to have miscarriage was between 13-18 years and 35-45 years.The ratio was higher in teenage girls(35%) and middle aged women(35%).

The lower class was found to suffer more with the highest ratio of 45%.Middle class was found to be less affected with the ratio of 20%.

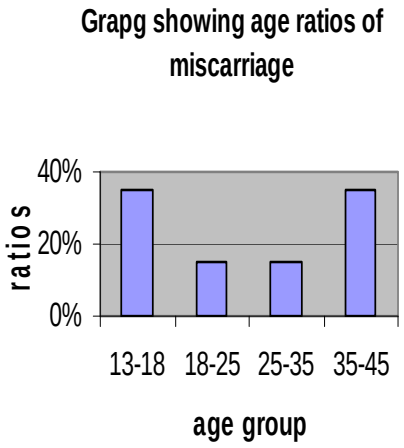

Figure 1: shows patients'age groups.

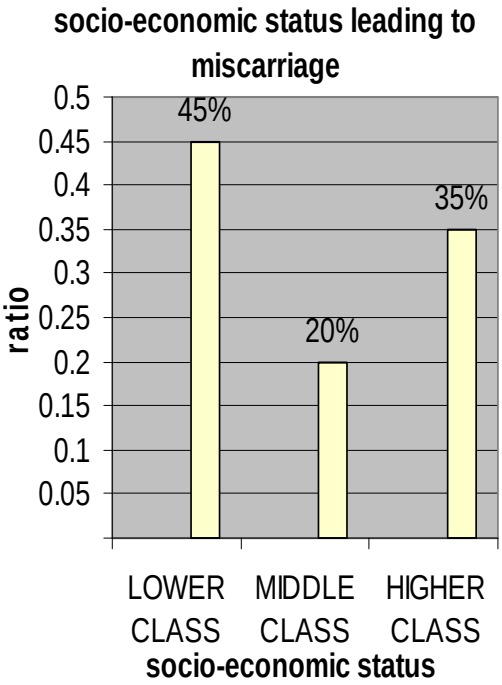

Figure 2: Effect of socio-economic status.

There were 20% patients found to undergo miscarriage due to hypertension. So high blood pressure is also one of the factors leading to miscarriage.22%(8/35) were found to be affected by miscarriage due to Intra-uterine devices they had used for birth control.6%(2/35) were found to be affected due to depression.

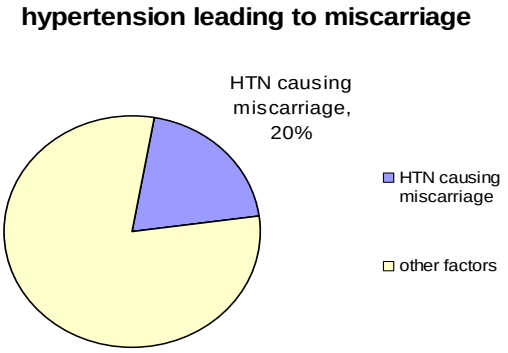

Figure 3:ratio of hypertension leading to miscarriage.

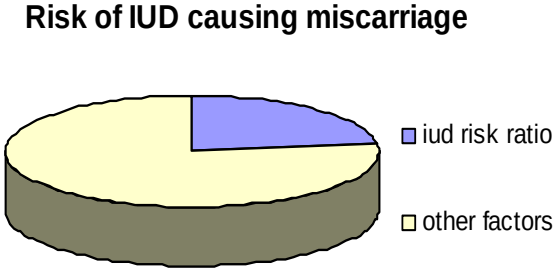

Figure 4: Risk of Intra-Uterine devices.

Sexually transmitted diseases also lead to miscarriage.3%(1/35) patients were found to be affected due to sexually transmitted diseases.Infection (baterial/viral) causing miscarriage ratio was found to be 3%.1 out of 35 patient was found to be affected due to infection. Ectopic pregnancy also leads to miscarriage.3%(1/35) patients were found to undergo miscarriage dur to ectopic pregnancy.As the number of births by C-section increases,it increases the risk of miscarriage of the latter pregnancies.8%(3/35) patients were found to suffer loss of pregnancy due to C-section history.23%(8/35) patients were affected due to poor diet.Malnutrition was found to be one of the major factor leading to miscarriage.23%(8/35)were found to suffer due to unknown reasons.

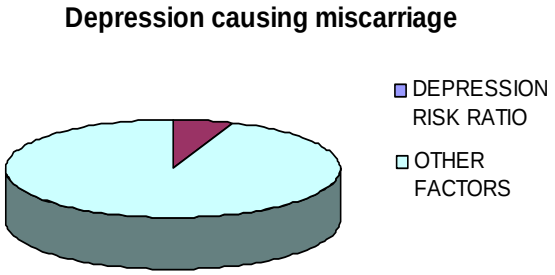

Figure 5.Hypertension ratio causing miscarriage.

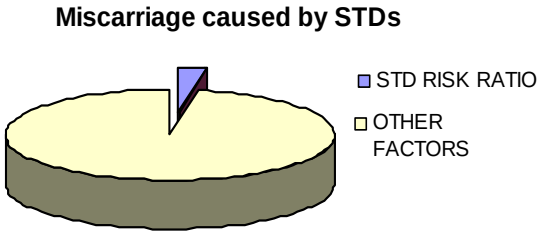

Figure 6:Ratio of miscarriages caused by STD.

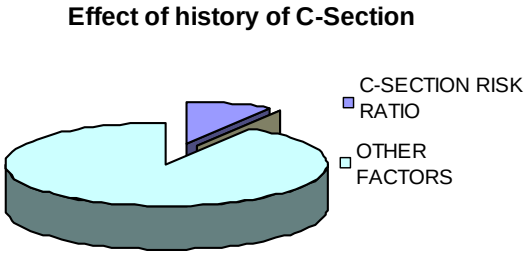

Figure 7: Effect of history of C-section causing miscarriage.

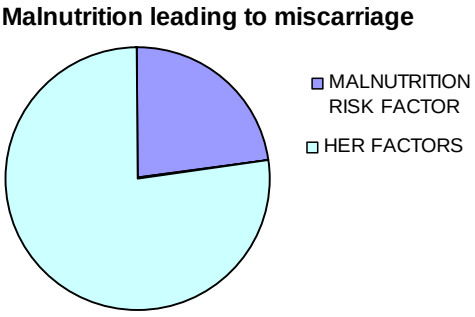

Figure 8: Mal-nutrition ratio causing miscarriage.

The factors which were found to cause miscarriage were depression, hypertension ,ectopic pregnancy, intra-uterine devices, malnutrition,infections(bacterial/viral), sexually transmitted diseases.It is not always possible to rule out the cause of miscarriage.There was a ratio of 23% cases with unknown cause of miscarriage.

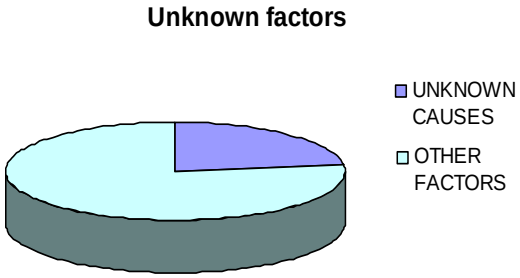

Figure 9: unknown causes ratio.

RECOMMENDATIONS:

Pharmacist should be appointed in hospital to ensure pharmaceutical care and patient counseling.Government should introduce programmes to educate and aware women about health problems and their gynecological concerns.Health professionals and leady health workers should be trained so that they could guide general public more efficiently regarding their health concerns.Education and lack of awareness is one of the major causes of ill-health.So women should be completely guided so as to avoid health related problems.Basic health care facilities should be provided.Patient care should be improved.There should be proper patient counseling.Complete medical history of patient should be asked.Role of pharmacist should be improved in pharmaceutical care.

CONCLUSION:

A miscarriage is any pregnancy that ends spontaneously before the fetus can survive. The factors which were found to cause miscarriage were depression ,hypertension, ectopic pregnancy, intra-uterine devices,

malnutrition, infections(bacterial/viral),sexually transmitted diseases.It is not always possible to rule out the cause of miscarriage.There was a ratio of 23% cases with unknown cause of miscarriage.In Pakistani society,we have need to improve the dietary habits of our women.Most of the women are anemic.The dietary deficiencies frequently lead to miscarriage.Depression is also one of the cause of miscarriage.Intra-uterine devices used for birth control can also lead to miscarriage.

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